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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/330,909	06/11/99	WOLFF J	MIRUS.011.01

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EXAMINER	
WOITACH, J	
ART UNIT	**PAPER NUMBER**
1632	5

DATE MAILED: 12/09/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/330,909	Applicant(s) Wolf et al.
	Examiner Joseph Woitach	Group Art Unit 1632

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-20* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-20* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The specific reference to the prior application must be in the form of a sentence (37 CFR 1.78) .

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)).

Nature of the invention. The claims are drawn to methods of gene therapy.

Breadth of claims. The claims are extremely broad, encompassing delivery of any and all nucleic acids to any cell in any portion of the cardiac tissue to treat any disease.

Guidance in the specification. The specification provides guidance on the use of two commercially available reporter DNA plasmid constructs. The specification does not give specific guidance regarding the use of other genes nor other promoter sequences, nor which gene and promoter should be used to treat which disease.

Predictability of the art. The physiological art in general is acknowledged to be unpredictable (MPEP 2164.03). Since the applicants have not disclosed other nucleic acids encompassed by the claims, there is no way to predict efficiency of delivery to nor expression in the cardiac tissue. Further, because the specification does not disclose an expected effect of introducing the nucleic acid, nor what cellular material it expects to modify, the claims encompass any change in the cell.

State of the prior art. At the time the invention was made, successful implementation of gene therapy protocols was not routinely obtainable by those skilled in the art. This is reflected by two subsequently published reviews. Verma et al. teach that as of 1997, "there is still no single outcome that we can point to as a success story" (p.239, col. 1). The authors go on to state, "Thus far, the problem has been an inability to deliver genes efficiently and to obtain sustained expression" (p. 239, col. 3). Anderson (1998) states that "there is still no conclusive evidence that a gene-therapy protocol has been successful in the treatment of a human disease" (p. 25, col

1) and concludes, "Several major deficiencies still exist including poor delivery system, both viral and no-viral, and poor gene expression after genes are delivered" (p. 30).

Amount of experimentation necessary. Besides the general expectation that it will require years of further research to develop effective gene therapy (Anderson, p.30), it would require extensive research to understand the fundamental biology of the system. Applicants have described a method to introduce and express two plasmid DNA vectors, but essentially all of the work required to ultimately develop therapeutic methods has been left for others.

For reasons discussed above, it would require undue experimentation for one of ordinary skill in the art to use the invention in the breadth in which it is claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claim 1 is vague and indefinite in their recitation of "cardiac tissue". In the Merriam-Webster's Medical Desk Dictionary, cardiac is defined as "a: of, relating to, situated near, or acting on the heart, b: of or relating to the cardia of the stomach" (p. 99, col. 1). The

specification does not define this term, and so it is not clear whether this includes veins, muscle, stomach, or some combination thereof.

Claim 1 is vague and indefinite in its recitation of "vessel". A vessel could include a blood vessel, however a vessel could also include a bowl, tube or any other container to which the DNA is injected.

Claims 3, and 8 are vague and indefinite in its recitation of "inserting" because it has no antecedent basis.

Claim 6, 11, 14, 17 are confusing in its recitation of "viruses" because while a virus could contain nucleic acid, a virus is not a nucleic acid.

Claim 7 is vague and indefinite in its recitation of "nucleic acid modifies expression of cellular material" because it is unclear what modifications are expected and how the modifications are brought about. The nucleic acid may directly affect expression/translation of some genes (i.e. antisense-oligonucleotides), or indirectly modify DNA or protein structures (i.e. ribozymes), alter expression of other genes (i.e. expression of enhancer or inhibitory elements), or simply kill the cell by the presence of toxic levels of exogenous nucleic acid. Further, "cellular material" could include lipids, amino acids and other metabolites present in the cell which can not be expressed.

Claim 12 is vague and confusing in its recitation of "changing a predetermined volume of nucleic acid" because it is unclear what nucleic acid is being used or what volume is changed.

Claim 18 is incomplete because no process steps are present where "therapy" occurs.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Claims 1-17 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Hajjar *et al.* Hajjar *et al.* teach a method using a catheter-based technique to achieve generalized cardiac gene transfer *in vivo* and to alter cardiac function by over expression of phospholamban.

Claims 1-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Leclerc *et al.* Leclerc *et al.* teach a method to deliver foreign DNA to arteries in a rabbit atherosclerotic model using a balloon-catheter system. A DNA-liposome complex was optimized for transfection of the DNA into the area of interest.

Claims 1-20 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Isner *et al.* (US patent # 5,830,879). With respect to claims 3, 6, 8, 11, 14, 17, 18, 19, Isner *et al.* teach delivering a nucleic acid, including; a viral vector, a retro- or adeno-virus, an oligonucleotide. With respect to claims 1, 4, 9, 20, Isner *et al.* teach a method of delivery by a catheter (Fig 2; col.

8, line 25). With respect to claims 5, 10, 12, 13, 15, 16, Isner *et al.* teach delivery by means of pressure, incorporation into liposomes, and incorporation of hydrogel (col. 6, line 6). With respect to claims 2, 7, 18, Isner *et al.* teach a expression of a nucleic acid (col 12, line 52).

Claims 1-20 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Mann *et al.* (US patent # 5,922,687). Mann *et al.* teach a method of delivering a nucleic acid into the heart by establishing an incubation pressure which facilitates the uptake of nucleic acid by the cell. The disclosed process includes all the method steps recited in the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mann *et al.* (US patent # 5,922,687) in view of Morishita *et al.* Mann *et al.* teach a method of

intracellular delivery of nucleic acid via a catheter. Mann *et al.* teach to use a catheter to isolate the area for delivery and use pressure to increase the uptake of the nucleic acid, however they do not teach other methods to increase the uptake of the nucleic acid. Morishita *et al.* teach a method of nucleic acid delivery to arteries *in vivo,* demonstrating uptake and expression of DNA as; naked DNA, liposome complexes and HVJ/liposome complexes. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the methods of Morishita *et al.* to increase the efficiency and expression of delivery of a nucleic acid to cardiac tissue as described by Mann *et al.* One having ordinary skill in the art would have been motivated to deliver a nucleic acid to cardiac tissue in such a way to achieve expression or the desired effect of the nucleic acid. There would have been a reasonable expectation of success given the results of Morishita *et al.* to deliver nucleic acid to other tissues *in vivo*, where one of the tissues is cardiac tissue as taught by Mann *et al.*

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach, whose telephone number is (703) 305-3732. The examiner can normally be reached on Monday through Friday from 8:00 to 4:30 (Eastern time).

If attempts to reach the examine by telephone are unsuccessful, the examiner's supervisor, Jasemine Chambers, can be reached on (703) 308-2035. The fax number for group 1600 is 1(703)308-4242.

An inquiry of a general nature or relating to the status of the application should be directed to the group receptionist whose telephone number is (703) 308-0196.

Joseph T. Woitach

Bruce Campell

BRUCE R. CAMPELL
PRIMARY EXAMINER
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